

Preliminary Amendment

Applicant(s): Peixuan GUO et al.
Serial No.: Unassigned (*Int'l Appln No.: PCT/US 2003/039950*)
Filed: Herewith (*Int'l Appln Filed: 16 December 2003*)
For: pRNA CHIMERA

JC17 Rec'd PCT/PTO 16 JUN 2005**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

Listing of Claims

1. **(Original)** A polyvalent multimeric complex comprising a plurality of pRNA chimeras, at least one pRNA chimera comprising (a) a pRNA region and (b) a spacer region comprising a biologically active RNA, the spacer region covalently linked at its 5' and 3' ends to the pRNA region.
2. **(Original)** The polyvalent multimeric complex of claim 1 wherein the biologically active RNA is selected from the group consisting of a ribozyme, a siRNA, an RNA aptamer, an antisense RNA and a peptide nucleic acid (PNA).
3. **(Original)** The polyvalent multimeric complex of claim 1 wherein the RNA aptamer binds a cell surface receptor.
4. **(Original)** The polyvalent multimeric complex of claim 1 wherein the RNA aptamer binds an endosomal disruption agent.
5. **(Original)** The polyvalent multimeric complex of claim 1 wherein the RNA aptamer binds to a virus.
6. **(Original)** The polyvalent multimeric complex of claim 5 wherein the virus is an adenovirus.
7. **(Original)** The polyvalent multimeric complex of claim 5 wherein the virus comprises a polynucleotide that operably encodes a therapeutic agent.

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8. **(Original)** The polyvalent multimeric complex of claim 1 comprising a pRNA chimera comprising an RNA aptamer the binds a cell surface receptor; a pRNA chimera comprising an RNA aptamer that binds an endosomal disruption agent; and a pRNA chimera comprising a therapeutic RNA.
9. **(Currently Amended)** The polyvalent multimeric complex of claim 1 ~~any of the preceding claims~~ wherein the spacer regions comprise the same or different biologically active RNAs.
10. **(Currently Amended)** The polyvalent multimeric complex of claim 1 ~~any of the preceding claims~~ which is a dimer, a trimer or a hexamer.
11. **(Original)** A polyvalent multimeric complex comprising a plurality of pRNA chimeras, each pRNA chimera comprising (a) a pRNA region and (b) a spacer region comprising a biologically active moiety.
12. **(Original)** The polyvalent multimeric complex of claim 11 wherein at least one of the pRNA chimeras comprises a RNA aptamer bound to the biologically active moiety.
13. **(Original)** The polyvalent multimeric complex of claim 12 wherein the biologically active moiety bound to the RNA aptamer is not an RNA molecule.
14. **(Original)** The polyvalent multimeric complex of claim 13 wherein the biologically active moiety is a peptide, a protein, a nucleic acid or a virus.
15. **(Original)** The polyvalent multimeric complex of claim 13 wherein the biologically active moiety is an adenovirus.
16. **(Original)** The polyvalent multimeric complex of claim 15 wherein the adenovirus comprises a polynucleotide that operably encodes a therapeutic agent.

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17. **(Currently Amended)** A method for delivering a therapeutic agent to a cell comprising:
contacting the cell with the polyvalent multimeric complex of claim 1 ~~any of the previous claims~~, wherein a first pRNA chimera of the polyvalent multimeric complex comprises a therapeutic agent and a second pRNA chimera of the polyvalent multimeric complex comprises a biologically active moiety that specifically binds a component of the cell membrane, such that the polyvalent multimeric complex is taken up by the host cell.
18. **(Currently Amended)** The method of claim ~~18~~ 17 wherein the component of the cell membrane to which the polyvalent multimeric complex binds is a receptor, and wherein the polyvalent multimeric complex is taken up by the cell via receptor-mediated endocytosis.
19. **(Currently Amended)** The method of claim ~~18~~ 17 wherein a third pRNA chimera of the polyvalent multimeric complex comprises an endosomal disruption agent.
20. **(Currently Amended)** The method of claim ~~18~~ 17 wherein the third pRNA chimera comprises an RNA aptamer that binds the endosomal disruption agent.
21. **(Original)** The method of claim 20 wherein the endosomal disruption agent comprises an adenovirus.
22. **(Original)** The method of claim 21 wherein the adenovirus comprises a polynucleotide operably encoding a therapeutic agent.
23. **(Currently Amended)** A method for delivering a therapeutic agent to a cell comprising:
contacting the cell with a polyvalent multimeric complex of claim 1 ~~any claims 1-16~~, wherein a first pRNA chimera of the polyvalent multimeric complex comprises an adenovirus comprising a polynucleotide operably encoding a therapeutic agent, and a second pRNA chimera of the polyvalent multimeric complex comprises a biologically active moiety that specifically

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binds a component of the cell membrane, such that the polyvalent multimeric complex is taken up by the host cell.

24. **(Original)** The method of claim 23 wherein the component of the cell membrane to which the polyvalent multimeric complex binds is a receptor, and wherein the polyvalent multimeric complex is taken up by the cell via receptor-mediated endocytosis.

25. **(Currently Amended)** The method of claim 17 ~~any of claims 17-24~~ wherein the cell is present in a cell culture, a tissue, an organ or an organism.

26. **(Currently Amended)** The method of claim 17 ~~any of claims 17-25~~ wherein the cell is a mammalian cell.

27. **(Original)** The method of claim 26 wherein the cell is a human cell.